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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/744,882	11/08/96	ISNER	46963

DAVID G CONLIN
DIKE BRONSTEIN ROBERTS & CUSHMAN
130 WATER STREET
BOSTON MA 02109

HM21/0401

EXAMINER
GAMBEL, P

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 04/01/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/744,882

Applicant(s)

Isner et al.

Examiner

GAMBEL

Group Art Unit

1642



☒ Responsive to communication(s) filed on Jan 9, 1998

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1, 2, and 4-22 is/are pending in the application.

Of the above, claim(s) 2, 4, 7, 8, 11, and 19-22 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1, 5, 6, 9, 10, and 12-18 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. The location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1642, Technology Center 1600.

2. Applicant's amendment, filed 1/9/98 (Paper No. 8), is acknowledged.

Claims 1, 5, 12, 13 and 14 have been amended.

Claim 3 has been canceled.

Claims 1, 5, 6, 9, 10 and 12-18 are being acted upon as the elected invention.

Claims 2, 4, 7, 8, 11, 19-22 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected inventions.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

Upon reconsideration of applicant's arguments, filed 1/9/98 (Paper No. 8), in conjunction with the Isner/Asahara Katz-type declaration under 37 C.F.R. § 1.132, filed 1/16/98 (Paper No. 9); the previous rejections under 35 USC 112, first and second paragraphs, 102, 103 have been withdrawn.

Applicant's arguments rely upon the amended claims, drawn to specific phenotype of endothelial progenitor cells. The claimed limitations of CD34, tie-2 and flk-1 are met by the New Grounds of Rejection set forth herein.

4. Formal drawings and photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948 previously sent in Paper No. 6.

5. Claims 1, 5, 6, 9, 10 and 12-18 are rejected under 35 U.S.C. § 103 as being unpatentable over Noishiki et al. (Nature Medicine, 1996; of record) OR Wilson et al. (U.S. Patent No. 5,612,211) in view of

Fennie et al. (Blood, 1995) OR Schnuerch et al. (Development, 1993) OR Yamaguchi et al. (Development, 1993)

and in further view of

Shi et al. (J. Vasc. Surg. 1994; of record), Bikfalvi et al. (Leukemia, 1994; of record) OR Asahara et al. (Circulation, 1995; of record). The instant claims are drawn to methods of enhancing angiogenesis or blood cell formation with endothelial cells or endothelial progenitor cells.

Wilson et al. Teach the use of the combination of the appropriate cytokines such as FGF and stem/progenitor cells of interest encompassing endothelial cells in various research and therapeutic modalities (see entire document, including Summary of the Invention and Therapeutic Administration and Compositions). This reference is silent about the expression of endothelial-specific markers and the use of endothelial progenitors for ischemia per se.

Noishiki et al. teach transplanting bone marrow cells resulting in the inducement of capillary growth (see entire document). This reference teaches that the bone marrow has stem cells but does teach isolating endothelial progenitor cells themselves. The reference does not teach using exogenous cytokines per se, but does teach cytokines such as FGF as well as products from other cell types are important for endothelial growth. This reference is silent about the expression of endothelial-specific markers per se.

Therefore, each primary reference teaches administering the combination of cells and appropriate cytokines such as FGF to treat various disorders.

Fennie et al. teach the expression of flk-1 and CD34 on endothelial progenitor cells (see entire document).

Schnuerch et al. teach the expression of tie-2 on endothelial progenitor cells (see entire document).

Yamaguchi et al. teach the expression of flk-1 on endothelial progenitor cells (see entire document).

Therefore the expression of CD34, flk-1 and tie-1 were known markers for endothelial cell progenitor cells.

Shi et al. teaches the proof of fallout endothelialization from grafts which relies upon progenitor cells from the circulation and the applicability of this for endothelialization including angioplasty (see entire document).

Either Bikfalvi et al. OR Ashara et al. teach the importance of various angiogenic factors including their combination on angiogenesis in vivo, which was important for revascularization therapeutic strategies (see entire documents).

Given the knowledge that stem or progenitor cells were in the bone marrow and in the blood, the ordinary artisan would have isolated marrow or blood from the patient of interest to obtain endothelial progenitor cells and reintroduce such cells into said patients upon their need. In view of the art known expression of CD34, FLK1 and tie-2 as taught by Fennie et al., Schnuerch et al. and Yamaguchi et al. And given standard procedures to isolate cells of interest at the time the invention was made and the motivation to isolate and transplant progenitor/stem cells of interest, the ordinary artisan would have isolated endothelial progenitor cells expressing said antigens and transplanted said endothelial cells in ischemic patient in need. In addition, the clear teachings of the prior art of using various cytokines such as FGF to stimulate angiogenesis in combination with endothelial cells to provide the targets for such angiogenesis in ischemic patients provide additional motivation and expectation of success at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to isolate and administer endothelial progenitor cells as a therapeutic regimen to induce neovascularization in patients of need. It was known at the time the invention was made that such neovascularization relied upon endothelial cells, including progenitor cells and appropriate cytokines. It was known at the time the invention was made that autologous transplantation was important to avoid transplant rejection, as was well practiced in transplantation regimens at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. No claim is allowed.

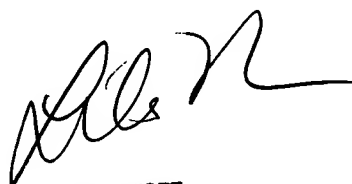
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee can be reached on (703) 308-2731. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [lila.feisee@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Phillip Gambel, Ph.D.
Patent Examiner
Group 1800
March 30, 1998



LILA FEISEE
SUPERVISORY PATENT EXAMINER